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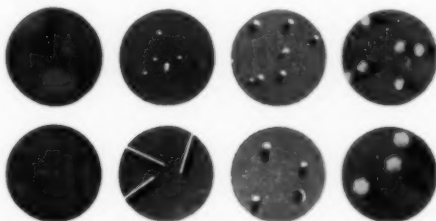


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Literature is available upon request.



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February 1961

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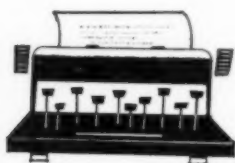
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Authors' Summaries...

Herbert J. Spoor, M.D., Ph.D.: EXTERNAL COD LIVER OIL THERAPY IN INFANTILE AND ATOPIC ECZEMA. (New York State Journal of Medicine. Vol. 60, No. 18, Sept. 15, 1960).

(From the Department of Medicine, New York Hospital)

In babies with infantile eczema, replacement of unsaturated oil and fatty acids on the involved skin via topical means, as an adjunct to elimination of known allergens "was almost universally rapidly curative," according to Dr. Spoor. He based his therapy on the fact that all such patients "show a relative deficiency of unsaturated natural oil and fatty acids in their skin emollients," and that replacement therapy topically improved their condition, provided that the oil added resembles that naturally present, particularly in terms of its unsaturation.

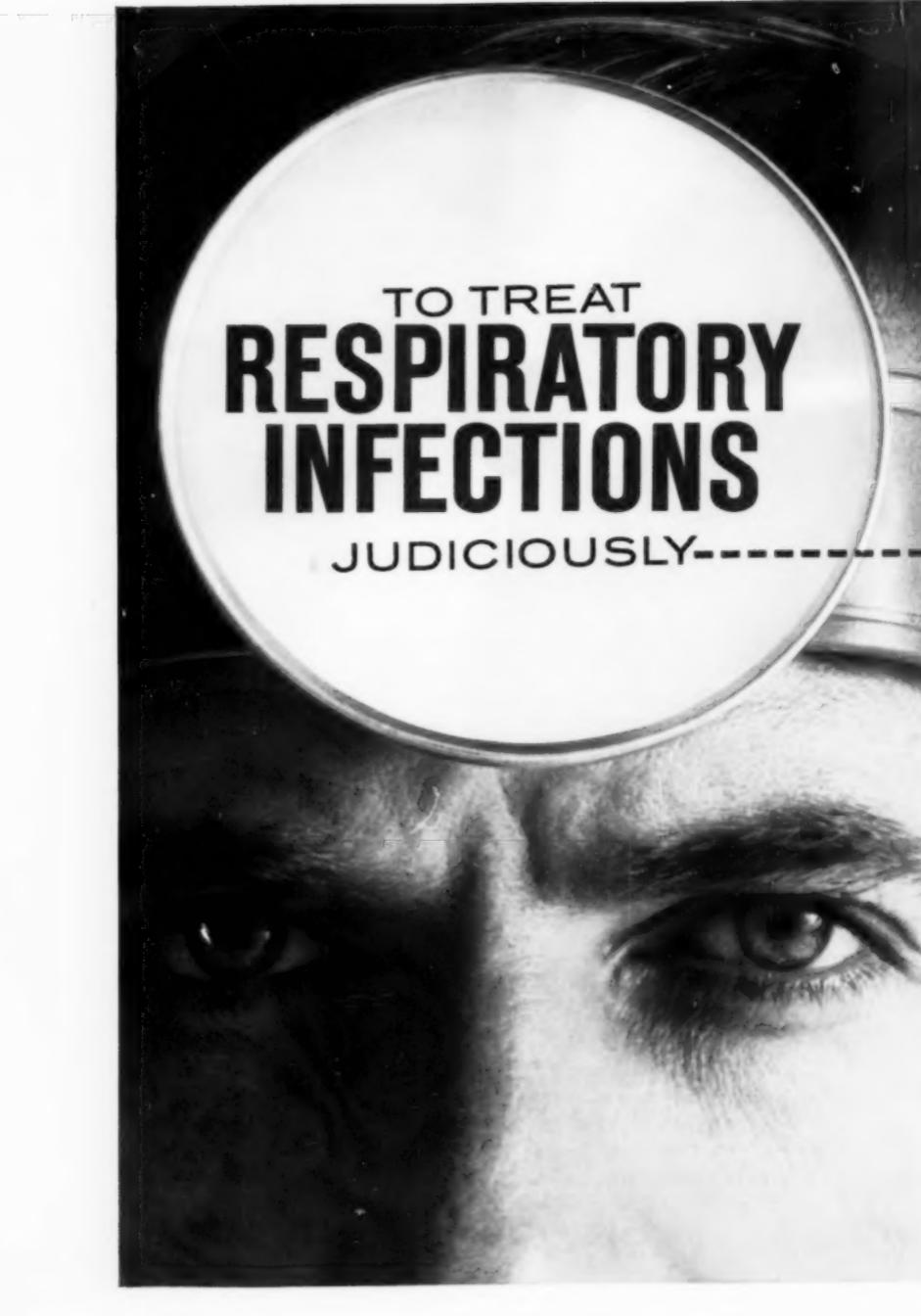
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Newman, C. G. H.: LONG-TERM FOLLOW-UP OF 32 PATIENTS IRRADIATED FOR THYMIC ENLARGEMENT IN INFANCY. (British Med. Jnl. 5165:34 Jan. 2 60).

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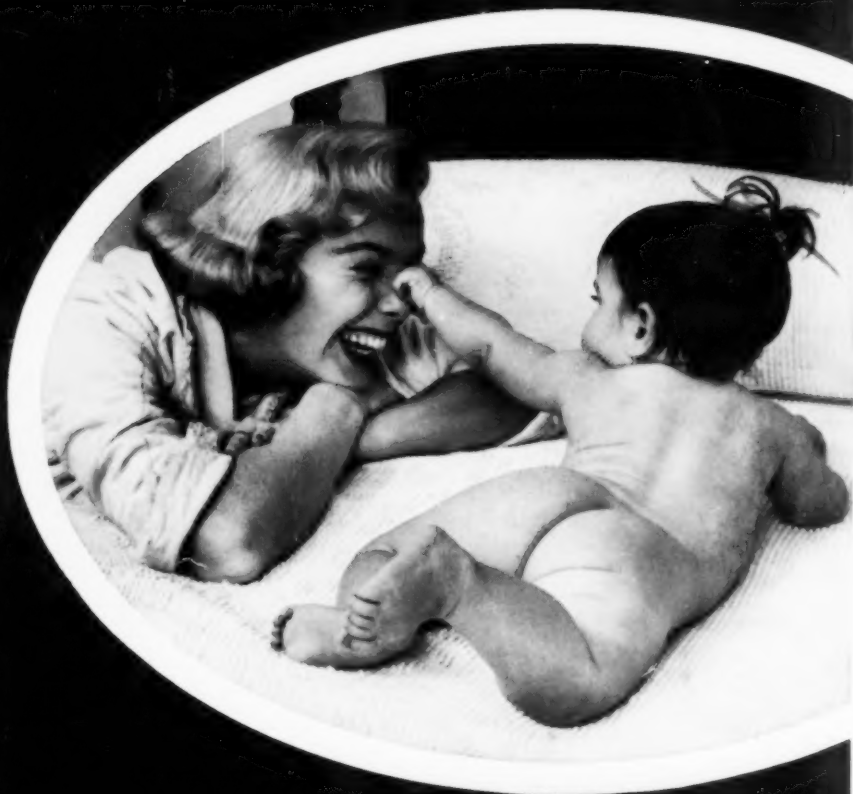
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References: 1. Soss, T. L., in Collect. Letters, Internat. Cor. Soc., Ophthalmologists & Otolaryngologists 3:177, Dec. 15, 1958.
2. Budetti, J. A., and Seydell, E. M.: *J. Kansas M. Soc.* 57:59, Feb., 1956.

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quest editorials

Athletics and the Child

R. A. MCGUGAN, M.D.*

Illinois

THE tempo and pressures of modern life are greatly increased over previous generations. This is one primary reason why we find more and more individuals failing to measure up to the demands of modern society, and a resulting greatly increased incidence of emotional and mental collapse.

There is no question but that physical well being has a great effect on emotional status. Educators recognize this and emphasize more and more the importance of health as a basic requirement for optimum benefit from educational experiences. And there is no question that the physically strong are less apt to succumb to emotional stress.

Obviously it is an obligation to us as pediatricians to encourage a maximum degree of physical well being in all children. This is such a basic concept that it is unnecessary to mention it to pediatricians. But there are considerations which make it of prime importance to us to take a more active part in the campaign for physical fitness, which is currently a subject of great activity among the professional physical educators.

Because of the emphasis on fitness by physical educators, and because much of this emphasis has been of too narrow focus and too vociferous a nature, pediatricians have repeatedly demanded to know what these people meant by fitness. "Fitness for what"? This was an attitude which was justified on our part at the time. But this is no longer true. The fanatics who thought only of muscular strength and paid no attention to the consideration of total fitness, are no longer heard, and a more mature and calmer majority has taken over. The emphasis now is on physical well being as a part of general fitness for life with all its stresses, physical, emotional and social; and with this approach, we as pediatricians can and should agree.

* Associate in Pediatrics, Northwestern University Medical School.

Where greater attention by the pediatric profession is needed is in the field of competitive athletics. It should be at once pointed out that very little conflict exists here between the medical profession and the physical educators. These men realize the value of a general program of physical activity embodying many sports and reaching the maximum number of children.

The emphasis on competitive athletics has come for the most part from well meaning but misguided lay people. With the great publicity emanating a few years ago from the proponents of physical fitness, many lay people became unnecessarily alarmed at the reported desperate plight of our children. It was stated baldly that many of our children were so physically unfit that they were in serious danger that they could not cope with the necessary demands of every day life. This, of course, was based on totally false premises, mostly on a series of tests of flexor strength, but the main effect was on lay people who were not equipped to evaluate the claims. As a result a great drive developed to provide more activity for children, to encourage athletics. An unfortunate result has been an undue emphasis on competitive athletics. The average parent, feeling that children need more physical activity, thinks first of team games, and without professional training in physical education he thinks of those two great American games, football and baseball.

Competition is, of course, a built-in part of modern life. Particularly to a child, competition is an everyday affair. He competes from the day he is born, against nature, against his parents, his siblings, his fellows and society itself. Since life itself embodies such competition, the child competes continuously, and added competition is quite frequently not only unnecessary but inadvisable. Unfortunately the lay person's idea of helping children is to organize competitive games, with the thought that boys need competition to make men of them, and without sufficient awareness of the many available, suitable, enjoyable and beneficial physical activities where competition is not so strong.

With this mistaken approach and activity by lay persons, greatly increased emphasis on competitive athletics has developed, and this is almost entirely shown in the form of organized football and baseball. Of these, of course, football is far and away the more dangerous, and probably the least beneficial. Of all forms of athletics, football is probably one of the least suitable, desirable or beneficial of team games, and certainly it is one of the most hazardous. When

we have football leagues being organized to promote this game for children of eight years and up, and when these games are played on a scheduled basis, something is wrong. The physical educators are not at fault—they would much prefer to handle children of this age on a non-competitive basis, with emphasis on activities which teach and develop fundamental skills and co-ordination. No such activities as Pop Warner Football and Little League Baseball have been fostered by professional physical education specialists.

Whenever one questions the advisability of such competitive sports for children and mentions the dangers involved, he is at once asked for figures to prove his statement. This is not an easy question to answer. All physicians see frequent injuries from football; all know of others. But no statistics are as yet available, and the lay individual, convinced of the importance of competitive athletics, does not readily accept what he considers to be only a wrong opinion voiced by a person he thinks to be too ready to coddle and protect the growing child. But despite the lack of formal studies, the facts remain and figures can be produced to demonstrate that football is not suitable as an activity for young children.

For example, the Wisconsin Medical Society made a study of insurance claims under state-wide compulsory high school athletic insurance program. It showed 3,984 of 6,200 injuries were due to football in a single year. The severity of these injuries is demonstrated by the fact that the cost of these was two-thirds of all the insurance costs combined, and $4\frac{1}{2}$ times as much as those from any other single activity. Other figures are available. One company reported that football in 7th, 8th and 9th grades accounted for 50 per cent of junior high school athletic claims, though only 10 per cent of junior high school youngsters took part in football. Another company stated that in 46,000 claims they found the younger the player the more likely he was to be hurt. The incidence of athletic injury in junior high school students was five times that of the 18 year olds.

Such figures as these are sobering. They cannot be brushed aside as inconsequential by even the most biased layman. And when we consider the future disability liable to result from fractures involving the epiphysis in these youngsters, the case against football below high school age becomes serious indeed.

A common fault among the non-professionals is failure to realize the difference between children and adults. The average person

thinks that children are quick, agile, react quickly and can therefore play games safely even though not experienced. This is, of course, a fallacy. Children's reflexes are not quick, their reaction time is slower; and inexperience produces a lack of judgment which can have serious consequences. All of us who have watched children play Little League ball have seen many batters struck by pitched balls. This is not because the pitchers are wild—it is because the batter is simply not able to react quickly enough to dodge, and because in many cases he does not realize, because he is inexperienced, how short a time he has to duck. This slower reaction time was discovered by Little League researchers, who found they had to move the pitcher farther from the plate. It is only fair here to state that any experienced pediatrician could have called their attention to this fact.

Dr. Conant, in his studies of the American educational scene, has remarked on the overemphasis on interscholastic athletic activity in junior high schools. This has undeniably been true and still is in some areas. Fortunately it is not sufficiently widespread to be a serious problem as yet. But there are still many schools where football is carried on as a means of providing material for the high school teams. And personal experience verifies the fact that where such football was abandoned in one city, the high school attempted to have the decision revoked.

Overemphasis has been one of the worst features of our football program in this country. Granted that it provides a source of funds which colleges can use to further a wider range of activities, it still is far from the ideal of sports as a builder of healthy active people. If college football is overemphasized for whatever reason, it does not follow that this emphasis should be passed on down even into junior high school.

As workers for the welfare of children, we are, and should be, interested in everything pertaining to the development of the child into a healthy adult. This means encouragement of physical activity rather than protecting the child against all harm. The pattern of adult life is laid down in childhood, and if we fail to develop in the child a love of physical activity and well-being, we will not have that well-being in adult life.

Competitive athletics is not the way to instill a love of playing in the child. The youngster who wants badly to make the team and is not able to do so, is not often able to produce the concentrated

drive necessary to better his performance. Instead, he is much more likely to retire into himself and to lose his incentive. Such a child will tend to become inactive and lose his desire to play games. With a "varsity" team in effect, he has no place to go.

Competition is perhaps the most serious deterrent to the development of a physically active population. Disappointment is not often a motivating influence to a child. Whenever competitive team games are promoted, there will be far more children left out than included. These "outsiders" are precisely those who should be receiving the attention, without which they are likely to become life long spectators, rather than players. We do not make "men" of boys by subjecting them to intensive competitive games. Instead, we drive a great many of them into an inactivity which they did not desire.

As physicians, we can do a great deal to reduce the emphasis on competitive athletics and to increase the physical health of our people. We can stress at every opportunity the ideal of greater physical activity for our children. We can encourage more games for more children. We can stress variety rather than concentration. We can urge the playing of games which can be continued in adult life. We can deplore any tendency to develop "varsity" type teams in the ages below high school. We can continually urge the de-emphasis of spectator sports and encourage participation. And we can continually, emphatically and repeatedly speak out against such games as football for young children and organized competitive sports for children below high school.

723 Elm Street, Winnetka, Ill.

The Incidence and Significance of *Candida* in the Stools of Marasmic Infants with Diarrhea

PROF. A. EL-GHOLMI, M.D.
Y. W. ABOUL-DAHAB, M.R.C.P.*
M. EL-ESSAWI, M.D.*

Egypt

PART I

GASTROENTERITIS still accounts for about 50% of the infant mortality rate in Egypt. That marasmus is the most important underlying factor in the morbidity and mortality of the disease was shown in a previous work.¹ Although oral, and to a lesser extent diaper thrush, are common in marasmic infants with diarrhea (the latter lesion being generally caused by fecal contamination of the skin), yet the incidence of the causative fungus in the stools and its relation to diarrhea in these infants are still a virgin soil for investigators in Egypt. Even abroad, this question does not seem to have provoked much interest. Hence the present investigation of the incidence and significance of *Candida* in diarrheal stools of marasmic infants, and of the problem of diagnosis of intestinal moniliasis.

MATERIAL AND METHODS

An unselected series of marasmic infants 1-12 months old, suffering from diarrhea, were investigated during the period May-August 1960. Excluded were infections with *Salmonella*, *Shigella*, enteropathogenic *E. Coli*, *E. Histolytica* and *G. Lambliia*. In addition to the usual clinical data recorded in cases of marasmus with gastroenteritis, those concerning oral or diaper thrush, present or past, were carefully sought. Rectal swabs were obtained from every case and oral and skin swabs from cases with clinical lesions.

BACTERIOLOGIC METHODS AND RESULTS

The bacteriologic investigations were undertaken by Y. Shaheen, G. S. Tawil, and Z. Maged, Bacteriology Department, Ein-Shams Faculty of Medicine. Details of their technique and results are under publication^{2,3}. A brief outline is hereby described.

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Rectal swabs were submitted to direct microscopic examination, cultured on Littman's agar treated with streptomycin and Sabouraud's agar. A growth of 50 colonies or more on Littman's medium was considered "profuse", of 10-50 colonies "moderate", and of less than 10 "scanty". Mouth and skin swabs and blood cultures were dealt with as described elsewhere².

The results of the incidence of candidas in the stools can be summarized as follows. Of the 172 cases examined, 92 had candidas of known pathogenicity in the stools. A *profuse growth* was obtained in 58 cases, in 20 of which the species was *C. albicans*, in 12 *C. stellatoidea*, in 22 *C. tropicalis*, and in 4 multiple species were isolated. In the rest the growth was scanty in the majority, and moderate in a few cases. Evidence of colonization of candida in the gut was present in 10 cases, all of which yielded a profuse growth on culture. Of 19 blood cultures, two were positive for *C. tropicalis*.

CLINICAL NOTES AND DATA

In all, 172 cases were examined; 35 were in the first degree of marasmus, 92 in the second and 45 in the third degrees. Gastroenteritis was severe in 71 cases, and mild in 101 cases. A history of congenital debility was obtained in 45 cases (26%). In most of the rest, underfeeding usually started the chain of events culminating in "marasmus". Other nutritional deficiencies present are shown in table 2. Parenteral infections were, as usual, common, but were assessed to be possibly of etiological importance in gastroenteritis in only a few cases, and to be occurring as a complication of marasmus in the great majority.

Oral thrush lesions were present in 38 cases. In several cases of proved thrush, the lesions consisted of a few small white patches scattered on a fiery red mucous membrane of mouth and adherent to it; such type of lesion may be easily overlooked. Diaper thrush lesions with the characteristic desquamated white epithelium at the margin⁴ were observed on 12 occasions. The total number of cases with thrush lesions was 43 (table 1, foot note), giving an incidence of 25%. This is higher than the usual incidence abroad, which even in maternity hospitals is below 20%; the general incidence of the disease being 4-5% in the neonatal period⁵. Perleche and atypical diaper rashes were seen in a number of other cases.

The distribution of the typical thrush lesions amongst infants in the various degrees of marasmus (table 1) shows that the incidence

Table 1: Relation of Severity of Marasmus to the incidence of thrush lesions and of profuse growth of candida from stools.

	1st.degree marasmus		2nd.degree		3rd.degree		Totals	
	Cases	%	Cases	%	Cases	%	Cases	%
No. of infants	35		92		45		172	
Incidence of oral thrush	6		20		12		38	22
" " " " " " " " " " " "	3		6		3		12	
Total No. of cases with thrush lesions	7	20	23	25	13	29	43	25
No. of pos. rectal swabs* in all cases	8	23	33	36	17	38	58	34
" " " " " " " " " " " "	5		19		9		33	77

* Percent of the number of infants under discussion

** The total is less than the addition of the 2 types of thrush because some cases had both types.

† By positive is meant a profuse growth of candida in culture.

of the lesions taken together, increases with the severity of marasmus, being 20% in the first, and 29% in the third degrees of marasmus. It may be pointed out, in passing, that of 10 cases that gave a history of neonatal thrush, 5 were immature at birth; 4 of the latter still had thrush at the time of examination, i.e. several weeks later.

The distribution of thrush lesions amongst the various age-periods, starting from one month (table 2) shows a maximal incidence from 1-3 months, and a marked drop in incidence from 7-12 months. This may be explained by the development of immunity to the disease after the neonatal period⁶, so that after infancy infection of the mouth with candida seldom if ever causes thrush lesions unless there are predisposing factors of which low immunity is one⁷. In our series of marasmic infants, although the incidence fell in the second half of the first year, it was still 21% at the 10-12 months period.

All oral thrush lesions were positive on culture, often with a profuse growth of one of the 3 species of candidas isolated during this work. On the other hand, a positive culture was obtained in 9 out of 10 cases with the characteristic diaper thrush lesion, whereas

of 6 cases with atypical perianal dermatitis only two were positive. Thrush lesions produced by the various species of candida were clinically indistinguishable.

CORRELATION OF CLINICAL AND BACTERIOLOGIC RESULTS

That the incidence of thrush is greater in marasmic infants is well-known. It was further shown in this work to be related to the severity of marasmus. If a heavy intestinal infestation with candida represents a disease condition and not a carrier state, then the incidence of such infestation should again go hand in hand with the severity of marasmus. This was shown to be actually so (table 1); the incidence in the second and third degrees of marasmus being 36% and 38% respectively, as compared with 23% in the first degree.

Moreover, cases with thrush lesions of the mouth and/or skin had by far the highest incidence of heavy intestinal infestation (77%). Whereas cases with only a past history of thrush had positive rectal swabs in 21%; and only 15% of cases with no thrush at all, present or past, were positive. That the fungus was living in the intestines and not just passing from the mouth in cases with oral thrush is shown by the profuseness of growth in the cases under discussion, 10 of which also showed evidence of colonization on direct examination of stools. Of these, 5 were in the second and 5 in the third degrees of marasmus; all were suffering from chronic diarrhea that was severe in five. Six had buccal thrush, one diaper thrush, and 3 were free from such lesions.

On the other hand, a profuse growth of candida failed to be obtained from the stools of 10 cases with oral thrush, in some of which the lesion was rather extensive. Hence the intensity of intestinal infestation, as assessed by the profuseness of growth, probably depends upon other factors in addition to the presence of oral thrush in a marasmic infant.

The age of the infant is probably one such factor. For the incidence of cases with profuse growth from stools showed the same trends of age distribution as that of the clinical thrush lesions (table 2), the lowest incidence being again at 10-12 months. In order to lend further evidence showing that this represents a true age incidence of the intestinal form of the disease irrespective of the presence of oral thrush, the incidence of profuse growth amongst cases with oral thrush of various ages was worked out (table 3). Seven out of nine thrush cases that failed to show a heavy intestinal

infestation fell in the age group of lowest incidence of moniliasis, viz, 10-12 months; the corresponding figures for cases with profuse growth being 6 out of 25. This also suggests that the same factor of relatively increased immunity to the fungus with age, mentioned before in connection with superficial thrush lesions, is again at work in intestinal moniliasis.

Table 2 : Age and Other factors in relation to incidence of profuse growth of candida from stools, and to incidence of thrush lesions.

	No. of cases	Pos. rectal swabs #		Thrush lesions	
		Cases	%	Cases	%
<u>Age:</u> 1 - 3 months	20	10	50	8	40
4 - 6 "	39	15	38	13	33
7 - 9 "	50	16	32	9	18
10 - 12 "	63	17	27	13	21
<u>Sex:</u> Male	79	19	24		
Female	93	39	42		
<u>Duration:</u> Acute	72	19	27		
Chronic *	100	39	39		
<u>Severity of diarrhea:</u> Severe	71	26	37		
Mild	101	32	32		
<u>Type of feeding:</u> Breast-fed	81	21	26	17	21
Artificially-fed or weaned	91	37	41	26	29
<u>Nutritional deficiencies:</u>					
Multiple	41	17	41		
Anemia **	47	10	21		
Rickets**	8	1			
Factors of Vit. B **	6	4			
Nutritional edema**	2	2			

By positive is meant a profuse growth of candida on culture.

* Of more than 15 days duration

** Occurring alone or almost so.

In corroboration with our thesis, bacteriologic examination revealed that in 8 of the 34 cases under discussion the species of candida isolated from the mouth was different from that of the stools.

Table 3: Incidence of profuse growth from stools
in cases with oral thrush at various ages *

Age in months	Cases with oral thrush		
	Profuse growth from stools	Negative or scanty growth	Total
1 - 3	3	1	4
4 - 6	10	1	11
7 - 9	6	0	6
10 - 12	6	7	13
Totals	25	9	34

* Only cases with recent thrush are included, to avoid errors in age of onset of the disease.

An assessment of the effect of other clinical data on the incidence of heavy intestinal infestation is shown in table 2. The female sex prevalence is curious, for no characteristic sex incidence is known of moniliasis. The duration of diarrhea seems to be significant: the incidence of heavy growth being 39% in chronic, as compared with 27% in acute diarrhea. This is in keeping with the results of our controlled trials of nystatin which showed a dramatic response in chronic diarrhea of monilial origin.² The severity of diarrhea, however, did not correlate with the incidence of infestation. Breast-fed infants had a lower incidence of intestinal infestation than those on other food, although thrush lesions were only slightly less frequent in the former. Cases with multiple nutritional deficiencies had a relatively high incidence of profuse growth from stools, but this may simply reflect the common association of such deficiencies with the third degree of marasmus. Whereas anemia unassociated with other specific deficiencies did not seem to be a factor. 4 out of 6 cases with mucous membrane manifestations of vitamin B complex deficiency yielded a profuse growth of candida. Only 4 cases gave a history of a significant course of treatment with antibiotics recently; two of them had heavy intestinal infestation.

DISCUSSION

A review of the literature shows that candidas are present in the stools of some 6-30% of healthy people⁸⁻¹⁰. In infancy the carrier rate of candida was reported by Japanese workers to be 40%.¹¹ In the present work the incidence in marasmic infants with diarrhea was 54%. In another publication,² the profuseness of growth in

culture was assessed by comparison with controls of healthy infants. According to the standards we concluded, the overall incidence of a "profuse growth" in the 172 marasmic infants of this series was 34%, a remarkably high figure when compared with the incidence of "significant quantity" of candida in the stools of healthy people (Schnoor, 1939).⁸ Yet his standards for "significant" were much lower than ours.

It should be borne in mind, however, that a profuse growth of candida in culture or the presence of many cells or spores on direct microscopic examination, i.e. a high degree of infestation should not be taken, alone, as an index of the etiologic role of the fungus. For it is known that proliferation of the latter may occur in sprue or other digestive disturbances.^{8,12} In the presence of any clinical evidence of moniliasis, however, diarrhea should suggest a cause-effect relationship.^{7,13,14} This suggestion should especially hold under such a condition of disturbed host-parasite equilibrium as debility.^{7,14,15,16} The effect of the latter was further illustrated by the marked difference in incidence of profuse growth in cases in the first degree of marasmus, as compared with cases in the 2nd and 3rd degrees.

It is noteworthy that three-quarters of cases with thrush lesions yielded a profuse growth from stools. Even cases with only a past history of thrush had a higher incidence of profuse growth than cases with no such history. Another observation emerging from this work was that the distribution of cases with intestinal infestation amongst the various age groups of infancy corresponded to that of thrush lesions, the incidence falling towards the end of the first year even in cases with oral thrush. Furthermore, breast-fed infants were less prone to heavy intestinal infestation than others. These results, taken together, afford clinical evidence for the significance of profuse growth of candidas from the stools of marasmic infants. On the whole, they confirm our statement, just quoted, that such a bacteriologic result in a debilitated infant with diarrhea is unlikely to imply a carrier state. That candida should not be regarded merely as a transient passer-by in the gut is further elucidated elsewhere².

We are aware, however, of the generally accepted recent American work¹⁷ which revealed that the presence of hyphae, mycelia or other evidence of colonization on direct microscopic examination of stools or other material denotes tissue invasion, and is hence one of the most reliable criteria in differentiating between the disease

and the carrier state. However, such evidence though almost conclusive, is not of common occurrence. It was present in only 10 cases (6%) in our series. If this criterion for a certain bacteriologic diagnosis of intestinal moniliasis were adhered to, without due consideration of the clinical side of the question, we would be at risk of missing or dismissing many infants whose only bacteriologic evidence of the disease is a profuse growth of candida from the stools. One of the purposes of this article is to show that we are in different diagnostic circumstances when dealing with undernourished infants with diarrhea. Like in other conditions in medicine, such as amaeic cyst-passers, a therapeutic test with a specific drug may be the only way to discern between the disease and the carrier state. A controlled trial of an antimonilial agent in the type of case under discussion was actually undertaken, and is the subject of another article.²

Apart from debility, other host factors may turn the balance in favor of candida. In general, the commonest are diabetes, pregnancy and severe infections. On the other hand, the most important factors enhancing the spread of the parasite in tropical and sub-tropical regions are heat, humidity and dust. Though antibiotics are generally thought to increase the incidence and morbidity of moniliasis, a review of the literature shows considerable divergence of opinion.

SUMMARY AND CONCLUSIONS

A study was undertaken of 172 marasmic infants with diarrhea, in 25% of whom thrush lesions were present. Cases with intestinal pathogens or severe parenteral infections were excluded.

Evidence of colonization of candida in the gut was shown in 6% of cases. Moreover, one third of cases yielded a profuse growth of candidas from the stools: *Albicans* 12%, *tropicalis* 13%, *stellatoidea* 7%, and multiple species in 2.3%. The overall incidence of heavy intestinal infestation with candida varied with the degree of marasmus. Remarkable was that such infestation followed a definite age incidence pattern that, though similar to that of thrush lesions, did not seem to depend on the presence of oral thrush. Evidence was presented that in marasmic infants with diarrhea and a profuse growth of candida from the stools, the chances of this indicating a disease condition (intestinal moniliasis) are considerable. Such chances are evidently greater if thrush lesions are present. Like in other conditions in medicine, the diagnosis of intestinal moniliasis should be based on both clinical and bacteriologic grounds.

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Phenethicillin in Pediatric Practice

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SINCE the discovery by Batchelor and his co-workers¹ that 6-amino penicillanic acid could be obtained by fermentation, other investigators have attempted the synthesis of new penicillins from this nucleus. One of these, phenethicillin potassium, is alpha-phenoxyethyl penicillin.² This semisynthetic penicillin has been reported to produce high blood levels on oral administration,³⁻⁶ to be more resistant to penicillinase degradation than other penicillins,⁷ and to be more readily absorbed from the gastrointestinal tract.^{3,4,6} Although these advantages of phenethicillin have been questioned by several highly qualified investigators,⁸⁻¹³ the clinical potentialities of the drug appear to be worthy of further investigation. In the present report, a clinical study of this new antibiotic is described, evaluating the efficacy of this orally administered agent in the treatment of various bacterial infections that are commonly encountered in children.

MATERIALS AND METHODS

Seventy-three children were included in the present investigation. They ranged in age from 2 to 15 years, and all were residents of an institution for the adoptive placement of normal children. All patients were screened by two pediatricians, and all were treated in an infirmary setting. The criteria used to determine inclusion were the presence of subjective clinical findings such as chills, malaise, sore throat, otalgia, cough, and chest pain, and objective findings such as fever, tachycardia, cervical adenitis, and degree of toxicity. The disease categories into which these cases fell, subdivided by age group, are shown in Table I.

Nose and throat cultures were obtained from each patient prior to initiation of therapy, as were cultures from other sites when indicated. Blood counts, urinalyses, sedimentation rates, and X-rays were obtained as the situation required.

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TABLE I
73 Pediatric Patients in Phenethicillin Trial, Classified by Disease
and Age Group

Disease	Age (years)	Age (years)	Age (years)
	2-5	6-10	11-15
Pharyngotonsillitis	24	14	21
Otitis media	4	0	2
Pneumonia	1	1	0
Infectious asthma	0	0	2
Abscess (cutaneous)	2	0	0
Generalized adenopathy	1	0	0
Impetigo	0	1	0
TOTALS	32	16	25

All cultures that resulted in bacterial growth were studied further for determination of sensitivity to antibiotics. The antibiotics used in these *in vitro* sensitivity tests were: phenethicillin, penicillin potassium G, streptomycin, erythromycin, chloromycetin, and tetracycline. These determinations were made by an independent laboratory, and the bacteriologic results were not made known to the investigators until after the conclusion of the study.

Phenethicillin was administered, as Chemipen[®], in tablet or syrup formulations, in dosages of 125 mg. or 250 mg. 3 times daily, as determined by age, weight, and severity of illness. Dosage thus determined ranged from 15 mg./kg./day to 35 mg./kg./day, the younger patients receiving the higher dosages. For this reason, the cases have been subdivided by age group in Table II, which lists each case individually, with clinical diagnosis, major pathogens detected on culture, sensitivity or resistance of the pathogen to phenethicillin and to penicillin G, dosage, duration of treatment, and clinical course.

Maintenance on, or discontinuance of, phenethicillin therapy and transfer to other antibiotics were based on clinical course and the presence of side effects. The majority of cases were treated from 7 to 10 days. The criteria for cessation of therapy were 24 to 48 hours of normal temperature and cessation and/or subsidence of clinical symptoms.

* Supplied by Dr. J. T. Groel of The Squibb Institute for Medical Research, New Brunswick, New Jersey.

TABLE II
Clinical and Laboratory Records of 73 Pediatric Patients

Case No.	Major pathogens	In vitro response* to phenethicillin	to penicillin G	Phenethicillin dose** and duration of Rx	Clinical course
PHARYNGOTONSILLITIS (AGE 2-5)					
1	Staphylococcus aureus	S1.S	S	125 mg., 10 days	Good: clear and asymptomatic in 4 days
2	Staphylococcus aureus	S	S	125 mg., 7 days	Good: clear and asymptomatic in 4 days
3	Staphylococcus aureus	S	S	250 mg., 9 days	Good: clear and asymptomatic in 7 days
4	Staphylococcus aureus	S	S	250 mg., 10 days	Good: afebrile and asymptomatic in 6 days
5	Staphylococcus aureus	S	S	125 mg., 6 days	Good: clear in 3 days
6	Staphylococcus aureus	S	R	125 mg., 3 days	Unsatisfactory: developed measles on day 4
7	Staphylococcus aureus	S	S	125 mg., 8 days	Good: clear in 6 days
8	Staphylococcus aureus	S1.S	S1.S	125 mg., 8 days	Good: clear in 6 days
9	Staphylococcus aureus	R	S	125 mg., 10 days	Good: clear and asymptomatic in 5 days
10	Streptococcus pyogenes	S	S	125 mg., 10 days	Good: clear and asymptomatic in 5 days
11	Diplococcus pneumoniae	S	S	125 mg., 6 days	Good: afebrile in 1 day, clear in 4 days
12	Staphylococcus aureus	S	S	250 mg., 10 days	Good: afebrile and asymptomatic in 2 days, clear in 5 days
	Streptococcus pyogenes	S	S		
13	Staphylococcus aureus	S	S	125 mg., 10 days	Good: clear and asymptomatic in 5 days
	Streptococcus pyogenes	S	S		
14	Staphylococcus aureus	S	S1.S	125 mg., 8 days	Good: clear and asymptomatic in 4 days
	Streptococcus pyogenes	S	S		
15	Staphylococcus aureus	S	S1.S	250 mg., 7 days	Good: clear in 3 days
	Streptococcus pyogenes	S	S1.S		

*Tested in standard sensitivity disks containing 20 u. phenethicillin. Key: S (sensitive), inhibition of growth in a zone in excess of 1.5 mm.; S1. S. (slightly sensitive), inhibition of less than 1.5 mm.; R (resistant), no inhibition of growth.

**Three times daily.

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Clinical and Laboratory Records of 73 Pediatric Patients

Case No.	Major pathogens	In vitro response* to phenethicillin	to penicillin G	Phenethicillin dose** and duration of Rx	Clinical course
16	Staphylococcus aureus	S1.S	S	125 mg., 6 days	Unsatisfactory; measles developed on day 4
	Streptococcus pyogenes	R	R		
17	Staphylococcus aureus	S	S1.S	125 mg., 7 days	Good; afebrile in 1 day, clear in 3 days
	Streptococcus pyogenes	S	S1.S		
18	Staphylococcus aureus	R	S	125 mg., 8 days	Good; clear in 5 days
	Streptococcus pyogenes	S	S		
19	Staphylococcus aureus	S	S	125 mg., 10 days	Good; clear and asymptomatic in 5 days
	Pseudomonas aeruginosa	R	R		
20	Staphylococcus aureus	S	S	125 mg., 10 days	Good; clear in 5 days
	Pseudomonas aeruginosa	S	S1.S		
21	Staphylococcus aureus	S	S	125 mg., 9 days	Good; clear and asymptomatic in 6 days
	Streptococcus pyogenes	S	S		
	Diplococcus pneumoniae	S	S		
22	Staphylococcus aureus	S	S1.S	250 mg., 8 days	Good; clear in 5 days
	Streptococcus pyogenes	S	R		
	Klebsiella pneumonia	R	R		
23	None recovered	—	—	125 mg., 5 days	Good; clear and asymptomatic in 3 days
24	None recovered	—	—	125 mg., 10 days	Good; clear in 6 days
PHARYNGOTONSILLITIS (AGE 6-10)					
25	Staphylococcus aureus	S	S1.S	250 mg., 5 days	Good; clear in 3 days
26	Staphylococcus aureus	R	S1.S	250 mg., 8 days	Good; clear in 4 days
27	Staphylococcus aureus	S1.S	S	125 mg., 5 days	Good; clear in 5 days
28	Staphylococcus aureus	S1.S	S1.S	250 mg., 7 days	Good; clear in 4 days
29	Staphylococcus aureus	S1.S	S1.S	250 mg., 10 days	Good; clear in 5 days

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TABLE II
Clinical and Laboratory Records of 73 Pediatric Patients

Case No.	Major pathogens	In vitro response* to phenethicillin	penicillin G	Phenethicillin dose** and duration of Rx	Clinical course
30	Streptococcus pyogenes	S	S	250 mg., 10 days	Good: clear in 3 days
31	Streptococcus pyogenes	S	S	250 mg., 10 days	Good: clear in 5 days
32	Proteus	R	R	250 mg., 7 days	Good: clear in 3 days
33	Staphylococcus aureus	S	S1.S	250 mg., 7 days	Good: clear and asymptomatic in 3 days
	Streptococcus pyogenes	S	S		
34	Staphylococcus aureus	R	R	125 mg., 9 days	Good: clear in 5 days
	Streptococcus pyogenes	S	S		
35	Staphylococcus aureus	S	S	250 mg., 7 days	Good: afebrile in 2 days, clear in 5 days
	Streptococcus pyogenes	S	S		
36	Staphylococcus aureus	S	S	250 mg., 6 days	Good: clear in 3 days
	Streptococcus pyogenes	S	S		
37	Staphylococcus aureus	S	S	250 mg., 2 days	Unsatisfactory: measles developed on day 2
	Streptococcus pyogenes	S	S		
	Pseudomonas aeruginosa	S1.S	S1.S		
38	None recovered	—	—	250 mg., 5 days	Good: clear in 4 days
PHARYNGOTONSILLITIS (AGE 11-15)					
39	Staphylococcus aureus	S	S	250 mg., 8 days	Good: clear in 5 days
40	Staphylococcus aureus	S	S	250 mg., 7 days	Good: clear in 1 day, afebrile in 3 days
41	Staphylococcus aureus	S	R	250 mg., 10 days	Good: clear in 4 days
42	Staphylococcus aureus	R	S	250 mg., 7 days	Good: clear in 5 days
43	Staphylococcus aureus	S	S	250 mg., 7 days	Good: clear in 5 days
44	Staphylococcus aureus	S	S1.S	250 mg., 7 days	Good: clear in 2 days
45	Staphylococcus aureus	S	S	250 mg., 10 days	Good: clear in 6 days
46	Staphylococcus aureus	S	S	250 mg., 7 days	Good: clear and asymptomatic in 3 days

TABLE II
Clinical and Laboratory Records of 73 Pediatric Patients

Case No.	Major pathogens	In vitro response* to phenethicillin	to penicillin G	Phenethicillin dose** and duration of Rx	Clinical course
47	Staphylococcus aureus	S	S	250 mg., 7 days	Good: clear in 3 days
48	Staphylococcus aureus	R	R	250 mg., 8 days	Good: clear in 5 days
49	Staphylococcus aureus	S	S	250 mg., 7 days	Good: clear in 3 days
50	Staphylococcus aureus	S	S	250 mg., 2 days	Unsatisfactory: measles developed on day 3
51	Staphylococcus aureus	S	R	250 mg., 7 days	Good: clear in 3 days
52	Staphylococcus aureus	R	R	250 mg., 8 days	Good: clear in 5 days
	Streptococcus pyogenes	S	S		
53	Staphylococcus aureus	S.I.S	S.I.S	250 mg., 7 days	Good: clear in 5 days
	Streptococcus pyogenes	S	S		
54	Staphylococcus aureus	S	S	250 mg., 7 days	Good: clear in 3 days
	Streptococcus pyogenes	S	S		
55	Streptococcus pyogenes	S	S	250 mg., 10 days	Good: clear in 6 days
	Pseudomonas aeruginosa	R	R		
56	None recovered	—	—	250 mg., 7 days	Good: clear in 3 days
57	None recovered	—	—	250 mg., 7 days	Good: afebrile and clear in 2 days
58	None recovered	—	—	250 mg., 5 days	Good: clear in 3 days
59	None recovered	—	—	250 mg., 7 days	Good: clear in 4 days
OTITIS MEDIA (AGE 2-5)					
60	Staphylococcus aureus	S.I.S	R	250 mg., 7 days	Good: clear in 4 days
61	Staphylococcus aureus	S.I.S	S.I.S	125 mg., 10 days	Good: clear in 6 days
62	Staphylococcus aureus	S	S	250 mg., 5 days	Good: clear in 4 days
	Streptococcus pyogenes	S	S		
63	Staphylococcus aureus	S	S	250 mg., 12 days	Unsatisfactory: afebrile in 3 days; transient diarrhea on day 5 cleared on change to chloromycetin and penicillin G
	Streptococcus pyogenes	S	S		
	Diplococcus pneumoniae	S	S		

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Clinical and Laboratory Records of 73 Pediatric Patients

Case No.	Major pathogens	In vitro response* to phenethicillin	to penicillin G	Phenethicillin dose** and duration of Rx	Clinical course
OTITIS MEDIA (AGE 11-15)					
64	Staphylococcus aureus	SLS	SLS	250 mg., 7 days	Good; clear in 4 days
65	None recovered	—	—	250 mg., 5 days	Good; clear in 3 days
PNEUMONIA (AGE 2-5)					
66	Streptococcus pyogenes	SLS	S	250 mg., 7 days	Good; lungs clear in 5 days
PNEUMONIA (AGE 6-10)					
67	Staphylococcus aureus	S	SLS	250 mg., 8 days	Good; lungs clear in 4 days
	Streptococcus pyogenes	S	SLS		
INFECTIOUS ASTHMA (AGE 11-15)					
68	Staphylococcus aureus	S	S	250 mg., 7 days	Good; clear in 5 days
	Streptococcus pyogenes	S	S		
69	Staphylococcus aureus	S	S	250 mg., 7 days	Good; clear in 5 days
	Streptococcus pyogenes	S	S		
CUTANEOUS ABSCESS (AGE 2-5)					
70	Staphylococcus aureus	SLS	R	250 mg., 7 days	Good; clear in 4 days; soaks applied
71	Staphylococcus aureus	S	S	250 mg., 7 days	Good; drained 3 days, clear in 10 days
GENERALIZED ADENOPATHY (AGE 2-5)					
72	Staphylococcus aureus	S	SLS	125 mg., 10 days	Unsatisfactory; further work-up showed infectious mononucleosis
IMPETIGO (AGE 6-10)					
73	Staphylococcus aureus	S	S	250 mg., 7 days	Good; clear in 7 days

RESULTS

Clinical

The clinical results of phenethicillin therapy in the present series of 73 cases was rated as good in 67. Of the 6 cases that failed to respond, 5 had demonstrable viral infection (measles in cases Nos. 6, 16, 37, and 50, and infectious mononucleosis in case No. 72) and only one case (No. 63) represented a bacterial infection. Phene-

thiicillin therapy was, therefore effective in 67 of 68 cases of bacterial infection. Moreover, there were no untoward side effects except, possibly, in case No. 63, and the drug was well accepted by all 73 children.

TABLE III
In Vitro Sensitivity of Pathogens in 73 Pediatric Cases

	Reaction ¹ to						Clinical results ²	
	Phenethicillin			Penicillin G			G	U
	S	S I	S R	S	S I	S R		
<i>Staphylococcus aureus</i>								
Alone	22	8	4	20	10	4	31	3 ³
With other organisms	15	2	3	12	6	2	17	3 ⁴
<i>Streptococcus pyogenes</i>								
Alone	3	1	0	4	0	0	4	0
With other organisms	22	0	1	18	3	2	20	3 ⁴
<i>Pseudomonas aeruginosa</i>								
Alone	0	0	0	0	0	0	0	0
With other organisms	1	1	2	0	2	2	3	1 ⁵
<i>Diplococcus pneumoniae</i>								
Alone	1	0	0	1	0	0	1	0
With other organisms	2	0	0	2	0	0	1	1
<i>Klebsiella pneumoniae</i>								
Alone	0	0	0	0	0	0	0	0
With other organisms	0	0	1	0	0	1	1	0
<i>Proteus</i>								
Alone	0	0	1	0	0	1	1	0
With other organisms	0	0	0	0	0	0	0	0
None found on culture	-	-	-	-	-	-	8	0

¹ Sensitivity disks were made in standard form, containing 20 units of phenethicillin. Grading criteria were: S (*sensitive*), inhibition of growth in a zone in excess of 1.5 mm.; S I (*slightly sensitive*), inhibition in a zone less than 1.5 mm.; R (*resistant*), no inhibition of growth.

² G, *good*; U, *unsatisfactory*.

³ Includes 2 cases of measles, 1 case of infectious mononucleosis.

⁴ Includes 2 cases of measles.

⁵ Includes 1 case of measles.

The efficacy of phenethicillin therapy in staphylococcal infections has been both praised^{6,8,9} and discounted.^{12,13} *Staphylococcus aureus*, coagulase positive, was found on culture in 54 cases (alone in 34 cases, associated with other pathogens in 20 cases—Table III). With the sole exception of case No. 63, every case of staphylococcal infection without viral complication was amenable to phenethicillin.

Several investigators report great efficacy for phenethicillin against beta-hemolytic streptococci.^{6,9} These pathogens were obtained from culture in 27 of the 73 patients in this series. Phenethicillin therapy was effective in 24 of these cases; of the 3 cases that did not respond, 2 developed measles (No. 16 and No. 37) and the third (case No. 63) represented a mixed infection.

Experience with 2 cases of infection with *Diplococcus pneumoniae*, both of which responded well, bears out the opinion of Bunn and Knight that phenethicillin is as effective as any other product for the treatment of pneumococcal pneumonia.¹⁴

Pseudomonas aeruginosa was recovered from 4 of these cases (Nos. 19, 20, 37, and 55). Except for case No. 37, which developed measles, clinical response to phenethicillin was rated as *good*. The single instances in which *Klebsiella pneumoniae* (No. 22) and *Proteus* (No. 32) were revealed on culture were also amenable to phenethicillin.

SENSITIVITY STUDIES

The results of the *in vitro* sensitivity tests are of considerable interest. Phenethicillin was often effective clinically despite *in vitro* findings of resistance or only slight sensitivity of the pathogen (Table III). Although *Klebsiella pneumoniae* and *Proteus*, for example, were found to be *resistant* to both phenethicillin and penicillin G *in vitro*, clinical response was rated as *good*. Also, when the 5 cases of viral infection are subtracted, the clinical effectiveness of phenethicillin is higher than that which would be indicated by the *in vitro* studies. It is also of interest that the clinical efficacy of phenethicillin was rated as *good* in each of the 8 cases in which no pathogens were recovered on culture.

In case No. 63 (otitis media), which has been referred to above, and which was the only case of demonstrable bacterial infection in this series that did not respond to phenethicillin therapy, all 3 pathogens recovered on culture (*Staphylococcus aureus*, *Streptococcus pyogenes*, and *Diplococcus pneumoniae*) were rated as *sensitive* to both phenethicillin and penicillin G. Although this patient was afebrile after 3 days on phenethicillin, there was a diarrhea on day 5, and the patient was transferred to intramuscular chloromycetin and penicillin G on day 6.

SUMMARY

Phenethicillin (Chemipen), a new semisynthetic oral penicillin,

was used as the original treatment in 73 cases of common infections of childhood. Clinical response was remarkably good. Excluding 4 cases of measles and a single case of infectious mononucleosis, in none of which was a satisfactory result to be expected, phenethicillin therapy was found to be effective in 67 of 68 cases. The drug was well accepted by all 73 children in the study.

ACKNOWLEDGMENTS

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Three Hydrocephalic Newborns — Each of a Successive Pregnancy of a White Female

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Indiana

W. BRENNER has considered the question of heredity in hydrocephalus and suggests that there is a dominate sex-limited inheritance, but this has not been proven. A review of the literature does not prove that there is a distinct hereditary element in hydrocephalus, but enough cases are on record to make one believe that the possibility of a repetition of these abnormalities cannot be denied.

Cause of such monstrosities is not known; a defective germ plasm is generally assumed. Theories that avitaminosis and endocrine abnormalities are causative have little, if any support. Our knowledge of the growth hormones of the anterior pituitary body is not sufficiently large to assign to this organ a role in the production of the monstrosities.

CASE REPORT: FIRST PREGNANCY

A 20-year-old woman was admitted to the hospital March 27, 1953, with an admitting diagnosis of "pregnancy, full-term primipara." Physical examination revealed normal heart, lungs and abdomen, with full-term pregnancy and a fetal heartbeat of 144. There was absence of nausea and vomiting, headache, leukorrhea or swelling of the extremities; the pregnancy had been uneventful and without complications. Blood-pressure was 134/65. Past history revealed nothing significant; there were no serious previous illnesses or miscarriages and the husband's health was good. The only abnormal laboratory report consisted of a positive gonorrheal smear.

The patient gave birth to a male weighing 7 lbs. 10 ozs., on March 27, 1953, at 3:30 p.m. Position was LOA and the presentation cephalic. Her child was a hydrocephalic with unassociated defects, and episiotomy was necessary. There was considerable molding of the head. A Bartholin abscess ruptured at the time of the repair of the episiotomy, and a smear of the foul-smelling

discharge sent to the laboratory, proved to be a gonorrheal pus. After delivery, both mother and babe were isolated from the obstetrical department. She received routine post-partum care. Antibiotics were advised for her infection, but she refused.

The patient was released from the hospital on April 1, 1953, with condition improved, and with a final diagnosis of "pregnancy living child, hydrocephalus delivered, and without associated defects, term birth, and gonorrheal Bartholinitis, left." Her child passed away Nov. 15, 1953, at the hospital with considerable enlargement of the original hydrocephalus and complications thereof.

We reassured the patient that a second hydrocephalic child in a subsequent pregnancy was extremely rare; it was explained to her that the possibility of the recurrence of hydrocephalus cannot be denied, but that it is extremely uncommon. We also pointed out that usually, when one child is hydrocephalic, the other children are normal, and that in general, unless there is a positive family history, she would run no greater risk in having additional children similarly affected than do other parents. She was advised to have a subsequent pregnancy.

COMMENT

Review of the world literature of the last 500 years reveals 23 instances in which one woman in successive pregnancies delivered two or more children with hydrocephalus alone. More than two were in combination with other defects. D. P. Murphy reported a case of spina bifida and hydrocephalus in each of three successive pregnancies. In his series of 275 families with one congenital malformed or defective child, 34 (12.4%) gave rise to one or more additional congenitally malformed members. He suggested that it was 24 times as likely for a second child as recorded per birth certificate to have a congenital malformation as the general population at large.

Butler reported a case of three children with spina bifida and two more who were hydrocephalic from the same mother in 1888. H. A. Wright reported a case of two babies both with myelocoele and hydrocephalus from the same mother in 1889. An anonymous Massachusetts physician reported a case of two hydrocephalic children from the same mother in 1933; Costelli reported two in one family, Gohlis reported six in one family and Peter Frank reported seven hydrocephalics from one mother.

Allingham reported one woman who in 12 pregnancies delivered three children who were hydrocephalic. Straub reported a man who married his niece; she delivered two hydrocephalic infants. Watterwald reports two male infants with hydrocephalus from the same mother. Wiener reports a case of the first and third child being hydrocephalic. H. R. Leland reported two hydrocephalic children and Murphy reported seven families having two hydrocephalic children. Murphy's study stated there was one chance in two that a second child would show the same congenital defect as the first.

Ford reported two hydrocephalic children from the same mother. His material consisted of 904 cases, which include all children with an encephalus, spina bifida, encephalocele and hydrocephalus born in the five largest maternity units in the state of Rhode Island during the years 1936 through 1952. W. Machado reported a case of one woman who in four pregnancies delivered two congenital hydrocephalic infants.

SECOND CASE REPORT

On September 3, 1954, the patient was admitted to the hospital with a full-term pregnancy. Her general health throughout her pregnancy had been excellent; there had been no significant weight gain nor history of virus infection during pregnancy, nor had there been radiation therapy, trauma or syphilis, or any other known complicating factors present. She submitted to x-ray pelvimetry on admission, which revealed a hydrocephalic child. It was concluded that the head would not be able to enter the inlet of the pelvis. Cesarean section was advised but was not agreed to by the patient. After four hours of hard labor, abdominal and rectal examination revealed the head engaged.

A female child in ROA position was delivered without episiotomy or forceps but there was considerable molding of the head, with occipito-frontal measurement of 21.5 cm. The mother was released from the hospital on Sept. 6, 1954, and made an uneventful recovery. The child was referred to the Walter Reed Memorial Hospital in Washington, D. C., where surgery was performed on the aqueduct of sylvius. The child survived approximately three months with continued enlargement of the head until it reached a diameter of 24 inches.

THIRD HYDROCEPHALIC CASE

A third hydrocephalic child was delivered and operated on at the

Indiana University Medical Center. It was first admitted to Riley Hospital 4-17-56 to 5-7-56, at age 1 month, with progressive enlargement of the head since birth. There were no associated defects. Past history revealed two siblings with the same condition. Ventriculogram was done which showed an atresia of the aqueduct of sylvius.

We performed a third ventriculostomy which resulted in a pronounced decrease in the head size with sinking of the fontanelle. The patient was discharged in good condition.

The hydrocephalic baby was readmitted 5-22-56 to 6-5-56 because of a recurrence of the progressive enlargement of the head. The patient had been seen in clinic and it was obvious that the third ventriculostomy was no longer functioning. He was therefore admitted for further workup. A ventriculogram was done which showed no evidence of function of the third ventriculostomy. This was followed by Torkolson's operation in which a tube was placed from the right lateral ventricle into the spinal subarachnoid space to the left of the spinal cord. The usual cisterna magna was not present, which necessitated the unusual position of the end of the tube. The patient tolerated the procedure well; the wound healed by primary intention. Upon the time of discharge the patient's head showed considerable decrease in size and the fontanelle was sunken.

The patient was then followed in the out-patient clinic. He seemed to be doing well until July 25, when pitting edema of the occipital scalp and bulging of the anterior fontanelle were noticed. However, examination revealed that the tube was still in position. The patient had a return appointment to the clinic on August 8, 1956. To this author's knowledge the baby lived three months.

DISCUSSION

Discussion with the late Dr. C. O. McCormick, Professor of Obstetrics and Gynecology at the Indiana University Medical Center, revealed that to his knowledge of the literature, no previous occurrence of three successive pregnancies each of which produced hydrocephalic children had been reported. The author's discussion with Dr. Nicholson Eastman of Johns Hopkins University in 1957 revealed nothing like this to his knowledge.

From the standpoint of the medical profession, repeated hydrocephalus in the same woman is extremely rare, but it does occur. Hydrocephalus *per se* is encountered in approximately one fetus

in 2,000 and accounts for some 12% of all malformations met with at birth. Thus the mathematical possibility of the same woman delivering three hydrocephalic children with unassociated defects in three successive pregnancies is almost an impossibility. Although associated defects are common and serious dystocia is the usual consequence, this patient delivered all three hydrocephalic children vaginally without serious dystocia. None of the three children revealed additional defects.

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Poison Control . . .

. . . ACTIVITIES IN NEW YORK CITY — 1960

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New York

DURING the year the Poison Control Center expanded its services qualitatively and quantitatively, focusing greater attention on the prevention of accidental poisonings. The control and prevention of lead poisoning was also a major focus of the Center's activities during 1960. The Poison Control Center continues, as originally, its regional function in serving many communities from Upstate New York and communities of adjacent States. Representatives from abroad, such as France and Australia, visited this Center with a view toward organizing similar facilities in their respective countries.

Incidents: (See Table I)

A slight increase is noted in the total number of incidents reported. The increase was chiefly in the "miscellaneous" group. Internal and external medications are responsible for the highest number of incidents reported.

The number of reported cases actually exceeds the number shown in this table since many incidents have as yet not been tabulated and included in the statistical report due to a shortage of clerical staff.

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Fatalities: (See Table II)

One hundred and fourteen (114) fatalities due to chemical poisonings were reported during the first ten months of the year. Nineteen (19) of these were in children under 6 years of age; 13 of the fatalities in this age category were due to lead poisoning, 2 to oil of wintergreen, 2 to aspirin, and one each to furniture polish and to Drano.

TABLE I
POISON CONTROL CENTER
Year End Report
January-October, 1960

TOXIC AGENT	SERVICE STATISTICS	
	Jan.-Oct. 1960 No. of Incidents	Jan.-Oct. 1959 No. of Incidents
Internal Medications	4,024	3,997
External Medications	750	744
Rodenticides	124	123
Insecticides	459	419
Household Articles:		
Disinfectants	151	173
Detergents	446	469
Polishes	115	113
Bleaches	352	313
Solvents	332	328
Cosmetics	419	400
Miscellaneous	1,275	1,386
TOTAL	8,447	8,465

The largest number of fatalities was due to barbiturate poisoning at ages 25-44, with the 45-64 group running close behind. This drug, in adults, was largely used with suicidal intent.

It is observed that lead poisoning in children under 5 years of age was responsible for more fatalities than any other condition or illness.

LEAD POISONING

Lead continues to be a frequent cause of poisoning in children under 5 years of age. In the first 10 months of 1960, 143 cases occurred and 13 deaths. In 1959 (annual figures), 171 cases were reported, 12 of which terminated fatally.

TABLE II
 POISON CONTROL CENTER
 Year End Report
 January-October, 1960

TOXIC AGENT	FATALITIES						Age	
	0-5	6-14	15-24	25-44	45-64	65 and Over	Un-known	Total
Barbiturates	—	—	1	6	10	5	3	25
Lead	13	—	—	—	—	—	—	13
Narcotics	—	—	5	8	1	—	1	15
Sleeping Pills	—	—	—	3	4	2	—	9
Oil of Wintergreen (Methyl Salicylate)	2	—	—	—	1	—	—	3
Aspirin	2	—	—	—	1	—	—	3
Digitoxin	—	—	—	—	1	1	—	2
Anacin	—	—	—	—	1	—	—	1
Sparine & Barbiturate	—	—	—	—	—	1	—	1
Atropine	—	—	—	—	1	—	—	1
Demerol	—	—	—	—	—	1	—	1
Sodium Fluoride	—	—	1	—	—	—	—	1
Cyanide	—	—	—	—	1	—	—	1
Lighter Fluid	—	—	—	1	—	—	—	1
Furniture Polish	1	—	—	—	—	—	—	1
Ammonia	—	—	—	—	—	1	—	1
Drano	1	—	—	—	—	—	—	1
Zonite	—	—	—	1	—	—	—	1
CN Disinfectant	—	—	—	—	—	1	—	1
Methyl Alcohol	—	—	—	1	—	—	—	1
Quinine & Turpentine	—	—	—	1	—	—	—	1
Unknown Drugs	—	—	2	15	7	4	1	29
Plastic Bag	—	—	—	—	1	—	—	1
TOTAL	19	—	9	36	29	16	5	114

As in previous years, there was a concentration of cases in three districts in Brooklyn: Red Hook, Fort Greene and Bedford. The Morrisania District showed the highest concentration in the Bronx.

The seasonal distribution of lead poisoning is also of interest with nearly 65% of the cases occurring during the months of July, August, September and October.

TABLE III
LEAD POISONING CASES
JANUARY-OCTOBER, 1960
Age (Years)

RACE AND SEX	Cases	Under 2	2	3	4	5	6 & Over	Child Age Unknown
<i>White</i>								
Male	5	—	5	—	—	—	—	—
Female	5	2	2	1	—	—	—	—
<i>Non-White</i>								
Male	33	11	15	6*	1	—	—	—
Female	23	5*	12**	5	1	—	—	—
<i>Puerto Rican</i>								
Male	37	11*	15**	6	3	2*	—	—
Female	37	5	19*	4*	3	3	3	—
<i>Race Unspecified</i>								
Male	3	1	1	—	—	—	—	1
Female	—	—	—	—	—	—	—	—
TOTAL	143	35	69	22	8	5	3	1

*Includes 1 fatality
 ** " 2 fatalities
 *** " 3 fatalities

TABLE IV
LEAD POISONING FATALITIES
JANUARY-OCTOBER, 1960
Age (Years)

RACE & SEX	Cases	Under 2	2	3	4	5	6 & Over
<i>White</i>							
Male	0	—	—	—	—	—	—
Female	0	—	—	—	—	—	—
<i>Non-White</i>							
Male	3	—	2	1	—	—	—
Female	3	1	2	—	—	—	—
<i>Puerto Rican</i>							
Male	5	1	3	—	—	1	—
Female	2	—	1	1	—	—	—
TOTAL	13	2	8	2	—	1	—

In cooperation with the Bureau of Sanitary Inspections, the Bureau of Laboratories and the Bureau of Public Health Nursing in this Department, an epidemiological study has been launched in a two block area in the Red Hook District where the highest incidence of lead poisoning prevails. Public health sanitarians visit every household and take samples from the walls of rooms, window sills, walls of hallways and the paint from the fire escapes. A urine sample is also collected from children under 6 years of age in these households for the detection of coproporphyrin. All children with a 3 plus positive reaction are referred for a lead blood determination by the public health nurse who visits the home. Children having a blood level of 0.06 mg./100cc of blood are referred to a treatment agency for further investigation and possible treatment.

Armed with evidence, the Bureau of Sanitary Inspections will use the information obtained for possible court action against the landlords involved. Attempts will also be made to involve the paint industry and others concerned towards finding a practical solution to making these homes lead-free and safe for children to live in.

Since education is perhaps the most potent single weapon in accidental chemical poisoning prevention, a concerted effort was made during the year in this direction. In cooperation with the Bureau of Health Education and the Office of Public Relations, considerable public education was carried on. All media were utilized. The radio and television were used extensively and, following each program, thousands of requests for information were received and literature promptly disseminated to all who inquired. It may also be said, parenthetically, that public health nurses during their home visits, for whatever purpose, carry on a significant health education campaign in looking for hazardous conditions and alerting parents on the indicated corrective measures to be employed.

In order to further the control and prevention of lead poisoning, a Lead Poisoning Study Group was formed, consisting of medical, technical and nursing administrators in the Department of Health. This group meets regularly to determine the best possible areas of approach to this problem.

Attempted Suicides in Adolescents: Over 100 attempted suicides by chemical means (nonfatal) were reported to the Center

during this period in adolescents, ranging from 10 years to 20 years of age. There was a preponderance in the female and many came from disorganized homes. Each case was investigated and referred for further psychiatric care.

Reporting of Side Reactions: During the year, greater attention was given to the reporting of side reactions by physicians, and particularly toxic reactions following the use of new drugs. The New York Academy of Medicine endorsed and approved the Department's suggestion that physicians report all side reactions to the Poison Control Center. Approval and endorsement were also obtained from all the local county medical societies and the Coordinating Council of the local county medical societies. In addition, this request was published through the societies' bulletins, and communications were addressed to the secretaries of various sections of the New York Academy of Medicine, such as the Section on Internal Medicine, the Section on Dermatology, and so forth.

REPORTING OF BLOOD DYSCRASIAS

The New York City Poison Control Center volunteered to the Subcommittee on Blood Dyscrasias, Council on Drugs of the American Medical Association, to use its network of Poison Control Officers to obtain reports of such incidents and to submit the reported incidents to the Subcommittee. Poison Control Officers as well as practicing physicians anywhere in the State were solicited to report such incidents to this Center. Forms for these reports have been distributed by the Center.

The reporting of a drug as the suspected cause of a dyscrasia, even though not conclusive evidence, would be exceedingly helpful to the Subcommittee. The August 15, 1959 issue of the *Journal of the American Medical Association* (vol. 170, p. 1931) carries an editorial comment about this registry. It aptly states that:

"The accumulation of a larger number of cases will make it possible to determine with greater certainty whether a causal relationship exists. The untoward side-effect of many of the newer therapeutic agents may not become apparent until the drug has had wide distribution. It is hoped that the registry can serve a useful purpose by alerting physicians and that they, in turn, will report all cases in which they suspect such a possibility. The success of the project will depend therefore on the cooperation of the physicians of the United States."

Plastic Bag Hazard: It is very gratifying to relate that no fatalities were reported this year resulting from the use of plastic bags. This is undoubtedly due to the concerted health education campaign carried on by the Department of Health and the exemplary cooperation received from industry.

Garden Hazards: This Center is frequently consulted about animal poisonings. Roy K. Imhoff, D.V.M., of the Animal Medical Center (Speyer Hospital for Animals), New York City, reported to the Center the death of a cat in the ingestion of an azalea of the Kurume variety. The Kurumes are hybrids of three species. The azaleas are all of the *Rhododendron* genus, as is the plant commonly known as the rhododendron. The poisonous principles found in this group are reported to be arbutin, ericolin, and andromedotoxin.

Various members of the plant family Ericaceae have from time to time caused loss in domestic and wild animals. All such plants which were carefully investigated have been shown to contain a resinoid poisonous principle which has been crystallized and partially characterized. It is given the name andromedotoxin. Possibly other active principles are present as well. According to the literature, the chief effect of andromedotoxin is the paralysis of the motor nerve endings, particularly the phrenic ones. It also has a direct action on striated muscle, causing stimulation followed by paralysis of vagal nerve endings and injury to the conducting tissue of the heart. Symptoms in sheep include depression, weakness, staggering, salivation, nausea, and irregular respiration. Postmortem examination reveals no characteristic lesions.

Although the Center's local experience with children has not been too alarming, according to the literature, the potential hazards in the garden are very frightening. Parents should impress on children, particularly very young ones, not to nibble or chew on anything but known foods. The random ingestion of leaves, berries, roots, and fungi is fraught with danger.

Poison Control Center Technical Advisory Committee: The Poison Control Advisory Committee met during the year. Among the subjects discussed was the Treatment of Organic Phosphate Poisoning. It was related that an effective antidote 2-PAM has been developed for the treatment of parathion poisoning but that the product is not now available for general use. Pharmaceutical houses which manufacture this antidote were contacted and the

plea was made that the drug be manufactured for general use. A supply was made available to the Poison Control Center for experimental clinical trial.

The Technical Advisory Committee also discussed the subject of side reactions and the efforts of the Poison Control Center in obtaining such information and working closely with the Food and Drug Administration were enthusiastically endorsed.

Education of the Medical and Nursing Professions: Educational activities are directed at all levels and are an integral part of the function of the Poison Control Center.

At a meeting of the Executive Committee of the New York branch of the American Academy of Pediatrics, at which its President-Elect was present, the prevention program of the New York City Poison Control Center was outlined as a model in the overall accident program of which poisoning is but a part. It was recommended that a network of poison control officers be utilized in effect as accident prevention officers and a roster of the poison control officers of New York City was provided to the American Prevention Chairman of the Academy of Pediatrics.

The authors participated in a Panel Meeting on Therapeutics, sponsored by the Committee on Medical Education of the New York Academy of Medicine, and devoted to the subject of Causation, Epidemiology and Treatment of Common Poisonings. The panel took a dim view of some of the measures and beliefs currently employed and held in the treatment of poisonings, that is, antidotes, emesis, gastric lavage, cathartics and dialysis.

At the invitation of the Department of Medicine of the Columbia Presbyterian Medical Center, the medical director participated in a Symposium on Accidental Chemical Poisonings. The students of the third and fourth year classes and the entire Faculty of Medicine were in attendance. The subject elicited great interest and much audience participation.

A talk on poisonings was given to the pediatric staff and the student body of the Downstate Medical Center, State University of New York. The entire pediatric staff at Kings County Hospital were also addressed on poisonings.

Lead poisoning, including the epidemiology, pathogenesis and prevention, was the subject of a talk to the pediatric staff of the New York Medical College-Flower Fifth Avenue Hospital. Poison Control was again included as an elective subject for students

attending Columbia University School of Public Health. Both the Medical and Technical Directors of the Center are serving as resource consultants. During the period, the activities of the Poison Control Center were described at three orientation seminars for new professional employees in the Department.

Many requests are received from hospitals to address their medical staffs on the poisoning control program. Among them were The Springfield Hospital of Massachusetts, Bellevue Hospital, Maimonides Hospital, the Jersey City Medical Center, Flushing Hospital, Bronx Municipal Center, Jewish Hospital of Brooklyn, etc.

It is gratifying to note the increased interest in the subject of accidental chemical poisoning prevention which is being evidenced by medical staffs of hospitals, medical schools and schools of nursing. Physicians are requested to report promptly all accidental poisonings to the Poison Control Center and to alert their patients on the potential hazards of drugs and household preparations and on the need for safe storage and handling of such products.

Technical notices are also sent out periodically to the Poison Control Officers and to the profession relating to any particular hazards which may occur at any time and seasonally. The following notice for example was recently sent out to all staff physicians, to Poison Control Officers and to practicing physicians in general:

November 29, 1960

"In addition to fire hazards which should be eliminated, as described in a previous directive, other hazards exist associated with this otherwise very happy season.

"During the period, just before Christmas (tree trimming time), incidents involving tinsel, Christmas light bulbs, holly and mistletoe berries occur. On Christmas Day, (opening and eating of presents time), incidents occur involving toys, paints, clay, mothers' gift perfumes, children's cosmetics, etc. Immediately after Christmas, (tree dismantling time), light bulbs, artificial snow, accidental ingestion of Christmas gifts and decorations (plastic snow scenes) occur. Any leaf, flower or berry and any plants may be a potential hazard and children in the household should be prevented from eating such products. New and exotic plants find their way into the home with increasing fre-

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quency and physicians must alert parents on the danger of children ingesting such articles.

"Since the inception of the Poison Control Center, over 50 incidents of accidental ingestion of substances associated with Christmas trees were reported to the center. The age range was from eight months to seven years. The number was equally divided among the sexes.

"A variety of products were included in the accidental ingestions such as tinsel, poster paints, dye from paper toy umbrellas, voodoo perfumes, noma ink from typewriter sets, colognes, cobalt chloride from chemistry sets, glass Christmas bulbs, holly berries, modeling clay, tree lights, snow scenes, Christmas lights and a host of other substances, such as glues and cements, solvents used for paints, plastic kits, and cements for toys. Anything outside of food products coming into the home can be expected to be hazardous when eaten by children. This is especially true during the holiday season when there is a sudden influx of new and varied assortments of products added to the household environment.

"Physicians are requested to alert parents on the potential hazards of these substances to young children, and the need for the selection of nontoxic products and large smooth surface toys, which cannot be swallowed by young children. Parents should also be requested to inspect carefully the trees and the entire home to eliminate any existing fire hazards."

POISON CONTROL EXHIBIT

An exhibit on the operation of the Poison Control Center, prepared with a grant from Mead Johnson and Company, was shown at the Annual Meeting of the American Academy of General Practice, in Philadelphia, in March of this year.

This exhibit was also presented at the Spring Meeting of the American Academy of Pediatrics, in Atlantic City, the following month. Many in attendance stopped to view it and to express personal thanks for the "excellent" services rendered by the Center. Requests were also received for literature and pamphlets.

In June, at the Annual Meeting of the American Medical Association, the exhibit was again shown, at the invitation of the AMA. Here, too, considerable interest was indicated by those in attendance. Nearly all the physicians who viewed the

exhibit were especially interested in lead poisoning and inquired how lead poisoning occurs—"Where does the child get the lead and how does he eat it?" The need for professional education on the mode of occurrence and the natural history of lead poisoning was quite apparent.

INTERESTING CASE REPORTS

1. The Emergency Unit of the Poison Control Center received a night call for assistance from Cumberland Hospital on a three-week old child who was in coma after having his last formula feeding. It appeared that the child, by error, had been given a milky solution from a half-gallon jug. This solution turned out to be an insecticide emulsion. From the records of the Permit Division the home address of the manufacturer of the insecticide (who was also an exterminator) was obtained. This material could have been one of two products and by a process of elimination the proper one was ascertained. After two days on the critical list the child recovered. Both the nursing bottle and the half-gallon jug were procured as museum specimens and should prove helpful for teaching purposes.

In this case it was an adult member of the family who made up the insecticide in a jug. One wonders whether the Code penalties relating to labeling and transfer of substances from original containers should not be applicable also to parents.

2. The Poison Control Center was consulted by St. Luke's Hospital in the case of a serious phosphorous poisoning in a three-year old child. This call was received at night and both the medical and technical directors were called to provide some aid and guidance on the most recent effective management of phosphorous poisoning. The physician became particularly alarmed since the patient took a turn for the worse as was evidenced by kidney and possible liver damage. Since no specific antidote is available for phosphorous poisoning, the question of the suitability of hemodialysis was raised. Numerous calls in the city and out of town to authorities in this field disclosed that there had been no precedent for hemodialysis being done in a case of phosphorous poisoning, and no precise knowledge was obtained whether phosphorous was dialysable. The hospital was advised with regard to symptomatic therapy and close observation of the patient. Since the patient improved clinically, hemodialysis was not done in this case.

3. A two-year old sibling administered approximately one ounce of oil of wintergreen, which he obtained from a dresser in the bedroom, to his 7-month old brother. After obtaining the bottle, he climbed onto the railing of the crib and poured the contents into the infant's mouth. Following emergency treatment and hospitalization, generalized convulsions developed and the patient died soon afterwards in spite of further treatment. This is the youngest patient with methyl salicylate poisoning ever reported to this Center, and perhaps anywhere.

4. The advice of the Center was requested when a two-year old child ingested a plastic toy. The Center was questioned on the possible toxicity, and the information obtained from the manufacturer brings up some pertinent facts on plastics. The dangers associated with the misuse of this plastic has recently received deserved attention. However, the ingestion of plastics is not normally considered a hazard because to a large degree they are inert and have low toxicity. These observations refer to plastics per se, for example, polyethylene and the vinyl types. Sometimes as much as 60 per cent of a plastic product may be composed of adjuvants, such as plasticizers, pigments, and anti-oxidants.

In the present case the product involved contained barium and cadmium stearates. Both barium and cadmium are objectionable components of anything that might be ingested by a child. Manufacturers of products used by children are not yet completely aware of the necessity for detailed information when formulating their products. The saving grace in many of these situations is that the product may not be soluble when ingested and hence not readily absorbed. Reliance on this probability, however, is too risky. Alternative and safer constituents should be used.

5. An industrial chemical mix-up occurred which might have had the major proportions of a similar incident which had occurred previously in Brooklyn. This time, a shipment of hydrochloric acid was dumped into concentrated sulfuric acid at an electroplating plant in the Bronx. Fortunately, only 10 gallons of hydrochloric acid were delivered. The violent reaction acted as a warning to prevent delivery of the rest of the shipment. Three employees were hospitalized.

6. Another incident involving an industrial chemical was the breaking of a container of phenyldichlorophosphine destined for

Israel. The Poison Control Center contacted both Richmond, Virginia, and Chicago, Illinois, in a rapid effort to obtain immediate advice on the treatment of this unusual chemical hazard. Appropriate corrective measures have been recommended.

PUBLICATION AND REVIEW OF ARTICLES

The Poison Control Center also receives frequent requests from scientific journals, such as "Pediatrics," and others, for review of articles relating to poisonings. Several articles were also written for "Collier's Encyclopedia" and "Grolier's Encyclopedia" on Poison Control Centers and Accidental Chemical Poisonings.

During the year twenty briefs on Accidental Chemical Poisonings were published in the "New York State Journal of Medicine" and, recently, a series on accidental chemical poisonings reported to the New York City Poison Control Center were initiated on a regular monthly basis for *Archives of Pediatrics*.

EFFECTIVENESS OF THE PROGRAM

It is not possible at this time to relate precisely how many poisonings were prevented as a result of the efforts of the Poison Control Center. It may be said, however, with due modesty, that no other activity has received greater acceptance by physicians and the public.

125 Worth St., New York 13

(This is the fourth of a series of papers by Dr. Jacobziner)



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1. Clin. N. W. Pediatr. Clin. North America, Nov., 1954, pp. 349-362.

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